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S.I.S.S.A. Cattaneo, Antonino Covaceuszach, Sonia Lamba,
Dorian <120> Method for the humanization of antibodies and humanized
antibodies thereby obtained<130> PCT 84150<140> PCT/IT2004/000722<141> 2004-
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tcagctctca aatcccact gctgaccatc actaggaca cttccaagag ccaagtttc 240
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Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Thr Asn Asn
20 25 30

Asn Val Asn Trp Val Arg Gln Ala Thr Gly Arg Gly Leu Glu Trp Met
35 40 45

Gly Gly Val Trp Ala Gly Gly Ala Thr Asp Tyr Asn Ser Ala Leu Lys
50 55 60

Ser Arg Leu Thr Ile Thr Arg Asp Thr Ser Lys Ser Gln Val Phe Leu
65 70 75 80

Lys Met His Ser Leu Gln Ser Glu Asp Thr Ala Thr Tyr Tyr Cys Ala
85 90 95

Arg Asp Gly Gly Tyr Ser Ser Ser Thr Leu Tyr Ala Met Asp Ala Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ala
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gggaaatctc ctcagctcct gatctataat acagataacct tgcatactgg ggtcccatca 180
cgattcagtg gcagtggatc tggcacacaa tattctctca agataaacag cctgcaatct 240
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Glu Thr Val Thr Ile Glu Cys Arg Ala Ser Glu Asp Ile Tyr Asn Ala
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ser Pro Gln Leu Leu Ile
35 40 45

Tyr Asn Thr Asp Thr Leu His Thr Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Gln Tyr Ser Leu Lys Ile Asn Ser Leu Gln Ser
65 70 75 80

Glu Asp Val Ala Ser Tyr Phe Cys Gln His Tyr Phe His Tyr Pro Arg
85 90 95

Thr Phe Gly Gly Thr Lys Leu Glu Leu Lys
100 105

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20 25 30

Asn Val Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Gly Gly Val Trp Ala Gly Gly Ala Thr Asp Tyr Asn Ser Ala Leu Lys
50 55 60

Ser Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Ala Tyr Leu
65 70 75 80

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

Arg Asp Gly Gly Tyr Ser Ser Thr Leu Tyr Ala Met Asp Ala Trp
100 105 110

Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

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Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Glu Asp Ile Tyr Asn Ala
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Asn Thr Asp Thr Leu His Thr Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Phe Cys Gln His Tyr Phe His Tyr Pro Arg

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Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
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Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Ile Lys Glu Tyr
20 25 30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Gly Leu Ile Asp Pro Glu Gln Gly Asn Thr Ile Tyr Asp Pro Lys Phe
50 55 60

Gln Asp Arg Ala Thr Ile Ser Ala Asp Asn Ser Lys Asn Thr Ala Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Thr Ala Ala Tyr Phe Asp Tyr Trp Gly Gln Gly Thr Leu
100 105 110

Val Thr Val Ser Ser
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Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
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Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Arg Asp Ile Lys Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Val Leu Ile
35 40 45

Tyr Tyr Ala Thr Ser Leu Ala Glu Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln His Gly Glu Ser Pro Trp
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

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Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr
20 25 30

Thr Met Ser Trp Ala Arg Gln Thr Pro Glu Lys Arg Leu Glu Trp Val
35 40 45

Ala Tyr Ile Ser Lys Gly Gly Ser Thr Tyr Tyr Pro Asp Thr Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Ser Ser Leu Lys Ser Glu Asp Thr Ala Leu Tyr Tyr Cys
85 90 95

Ala Arg Gly Ala Met Phe Gly Asn Asp Phe Phe Pro Met Asp Arg

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105

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Trp Gly Gln Gly Thr Ser Val Thr Val Ser Ser Ala
115 120

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His Trp Tyr Gln Gln Lys Ser Gly Thr Ser Pro Lys Leu Leu Ile Tyr
35 40 45

Thr Thr Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Phe Tyr Ser Leu Thr Ile Ser Ser Val Glu Ala Glu
65 70 75 80

Asp Ala Ala Asp Tyr Tyr Cys His Gln Trp Ser Ser Tyr Pro Trp Thr
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Phe Gly Gly Thr Lys Leu Glu Ile Lys
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Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr
20 25 30

Thr Met Ser Trp Ala Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Tyr Ile Ser Lys Gly Gly Ser Thr Tyr Tyr Pro Asp Thr Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Ser Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Ala Met Phe Gly Asn Asp Phe Phe Phe Pro Met Asp Arg
100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala
115 120

<210> 38<211> 106<212> PRT<213> Homo sapiens<400> 38
Asp Ile Val Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Ser Ala Ser Ser Ser Val Ser Tyr Met
20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Lys Leu Leu Ile Tyr
35 40 45

Thr Thr Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
65 70 75 80

Asp Val Ala Thr Tyr Tyr Cys His Gln Trp Ser Ser Tyr Pro Trp Thr
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Phe Gly Gly Thr Lys Val Glu Ile Lys
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20 25 30

Tyr Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Leu
35 40 45

Gly Phe Ile Gly Asn Lys Ala Asn Gly Tyr Thr Thr Glu Tyr Ser Ala
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Lys Ser Lys Ser Thr
65 70 75 80

Leu Tyr Leu Gln Met Asn Thr Leu Gln Ala Glu Asp Ser Ala Ile Tyr
85 90 95

Tyr Cys Thr Arg Asp Arg Gly Leu Arg Phe Tyr Phe Asp Tyr Trp Gly
100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser Ala
115 120

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Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Ser Ser Val Thr Tyr Ile

20

25

30

His Trp Tyr Gln Gln Lys Pro Gly Leu Ala Pro Lys Ser Leu Ile Tyr
35 40 45

Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Asp Tyr Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu
65 70 75 80

Asp Ile Ala Thr Tyr Tyr Cys Gln His Trp Ser Ser Lys Pro Pro Thr
85 90 95

Phe Gly Gln Gly Thr Lys Val Glu Val Lys
100 105